REMARKS and ARGUMENTS

A. Claim Amendments

In addition to the amendments to the claims that are apparent above, claims 15-21, 56, 58, 62, 64, 69, and 71 have been cancelled as being drawn to nonelected subject matter.

B. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

The Office rejected claim 5 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

Specifically, the Office stated on page 2 of the Office Action that claim 5 recites species that are outside the scope of formula III of claim 3 and that there is insufficient antecedent basis for this limitation in the claim. Claim 5 has been amended to remove species that are allegedly outside the scope of formula III of claim 3.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

C. Claim Rejections under 35 U.S.C. § 103(a)

Claims 3-7, 10, 11, 28, 30, 31, 33, 34, 36, 37, 39, 50, and 99-101 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Baxter et al. (US 6,545,005 B1) (Baxter). Applicants respectfully traverse this rejection.

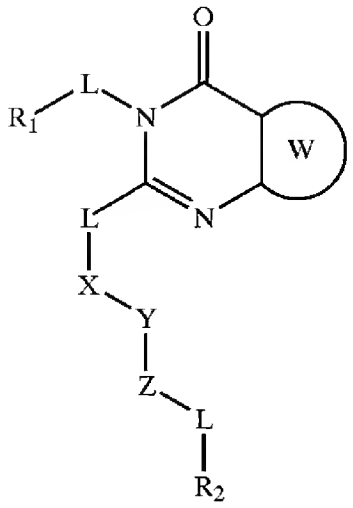
On page 3 of the Office Action the Office has asserted that generic formula II of Baxter encompasses the instant formula III. The Office has further asserted that although Baxter does not disclose additional species of a sulfonamide substituent at the 2-position, the formula II subgenus in column 31 provides sufficient teaching for one skilled in the art to select compounds of the instant formula III to agonize or antagonize hedgehog pathway. Applicants respectfully disagree and submit that the present claims are would not have been obvious over Baxter.

There is nothing in Baxter directing one to the presently claimed subgenus of compounds, nor that such compounds would be effective nuclear receptor modulators in general or farnesoid X receptor (FXR) modulators, in particular. The presently claimed genus of compounds is but a small subgenus of the genus disclosed in col. 31 of Baxter, as manifested in the following

recitation from col. 31 of Baxter in which the moieties other than those recited by the Office are displayed as strikethrough text:[1]

In embodiments wherein Y_1 and Z_1 are absent and X_1 comprises a pyrimidone, compounds useful in the present invention may be represented by general formula (II):

Formula II



wherein, as valence and stability permit,

R_1 represent[s] ~~H, lower alkyl,~~ aryl (e.g., substituted or unsubstituted)~~, aralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ heteroaralkyl)~~;

R_2[, represents ~~H,~~ lower alkyl, aryl (e.g., substituted or unsubstituted)~~, aralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ heteroaralkyl)~~;]

L, independently for each occurrence, is absent or represents ~~$-(CH_2)_n$ alkyl, alkenyl , alkynyl , $-(CH_2)_n$ alkenyl , $-(CH_2)_n$ alkynyl , $-(CH_2)_n O(CH_2)_p$,~~ $-(CH_2)_nNR_2(CH_2)_p$-;

X can be selected from ~~$-N(R_8)$, $-O$, $-S$, $-Se$, $-N=N$, $-ON=CH$, $-(R_8)N-N(R_8)$, $-ON(R_8)$, a heterocycle, or~~ a direct bond between L and Y;

Y can be selected from ~~$-C(=O)$, $-C(=S)$, $-S(O_2)$, $-S(O)$, $-C(=NCN)$, $-P(=O)(OR_2)$, a heteroaromatic group, or a direct bond between X and Z~~;

Z can be selected from ~~$-N(R_8)$, $-O$, $-S$, $-Se$, $-N=N$, $-ON=CH$, $-R_8-N-NR_8-$, $-ONR_8-$, a heterocycle, or~~ a direct bond between Y and L;

~~R_8, independently for each occurrence, represents H, lower alkyl, aryl (e.g., substituted or unsubstituted), aralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ heteroaralkyl-), or two R_8 taken together may form a~~

[1] R_1 and R_2, which are defined in Baxter identically but independently of each other has been split into two paragraphs for clarity.

~~4- to 8-membered ring, e.g., with X and Z, which ring may include one or more carbonyls;~~

W represents a substituted or unsubsituted [sic] aryl ~~or heteroaryl~~ ring fused to the pyrimidone ring;

p represents~~, inde~~ him ~~pendently for each occurrence, an integer from 0 to 10, preferably from 0 to 3~~;

and n, ~~individually for each occurrence,~~ represents ~~an integer from 0 to 10,~~ preferably from 0 ~~to 5~~.

As is apparent from the foregoing, the presently claimed genus of compounds is but a small subgenus of compounds encompassed by the description in col. 31 of Baxter and, indeed, is even a subgenus of the subgenus identified by the Office as R_1. R_2, and W can each be "substituted," but no specific substituents are identified.

There is nothing in Baxter giving reason to one of ordinary skill in the art to select such compounds. Baxter discloses but a single compound having a sulfonamide linkage (compound 14, spanning cols. 75-76) falling within the subgenus identified by the Office, but presents it merely as a synthetic example and does not otherwise identify it as being of particular interest. Significantly, this compound is not among those identified in the assay presented in col. 63 of Baxter. As recently reiterated in *Bayer Schering Pharma AG v. Barr Laboratories Inc.*, 91 USPQ2d 1569, 1573 (Fed. Cir. 2009), generalities or vague or non-existent guidance towards the claimed invention is insufficient to render a claim obvious; there must be some reason for the ordinary artisan to make the *particular* invention being claimed. Baxter provides no reason for one of ordinary skill in the art to select the particular subgenus of compounds presently being claimed.

In addition, Baxter fails to provide information from which one of ordinary skill in the art could expect that the presently claimed compounds would be nuclear receptor modulators or, in particular, FXR modulators. Baxter only discloses the use of small molecule compounds that agonize inhibition of hedgehog signaling in the regulation of repair and/or functional performance of a wide range of cells, tissues and organs having the phenotype of hedgehog gain-of-function. The mechanism of action of Baxter compounds of formula II is specific to signal transduction pathways regulated by a hedgehog family of genes, and only speculatively attributed to an activation of a hedgehog receptor. No utility or even potential utility was disclosed or suggested for Baxter compounds of formula II for use as quinazolinone modulators of nuclear receptors in general and (FXR) in particular, as disclosed in the present application.

Thus, the properties of the presently claimed compounds as FXR modulators could not have be predicted from Baxter.

With a reason to select the presently claimed compounds or the ability to predict their properties as nuclear receptor/FXR modulators, the presently claimed compounds cannot be obvious.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

D. Non-Elected Subject Matter

Method of use claims 84-98 currently stand withdrawn from consideration as being drawn to a non-elected invention. On page 4 of the Office Action the Office has requested cancellation non-elected claims or other appropriate action.

Pursuant to MPEP §821.04(b), if Applicants elect claims directed to a product that is subsequently found allowable, the withdrawn process claims that depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder. Upon rejoinder of claims directed to a previously non-elected process invention, the restriction requirement between the elected product and rejoined process claims will be withdrawn. Thus, if the product claims are found allowable, the non-elected method of use claims (withdrawn) should be rejoined.

Applicants respectfully submit that Withdrawn claims 84, 86-88, and 93-97 are amended to correct the claim dependency. Thus, method claims 84-98 as presented require all the limitations of the elected product (compound) claims, and the Applicants respectfully request their rejoinder.

In light of the all above arguments, Applicants respectfully request reconsideration and withdrawal of the rejections of the pending claims. If the Examiner believes it to be helpful, he is invited to contact the undersigned representative as indicated below.

Respectfully submitted,

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